REMARKS

Claims 104-115 have been canceled as directed to a non-elected invention. Claim 96 has been limited to actinomycetes as host cells. Support for this limitation is found, for example, on page 22 at line 24.

Double Patenting

All pending claims, claims 96-101, were rejected as obviousness-type double-patenting over:

claims 1-6 of U.S. Patent No. 6,399,382;
claims 5-12 and 15-21 of U.S. Patent No. 5,672,491; and
claims 32-38 of U.S. Patent No. 6,022,731.

In response to this rejection, terminal disclaimers with respect to these patents are enclosed. It is believed the double-patenting rejection is thereby overcome.

The Rejection Under 35 U.S.C. § 112, paragraph 1

All claims were rejected as assertedly not enabled for the scope of the claims. The Office acknowledges that the disclosure is enabling with respect to a method to modify *S. coelicolor* to contain a nucleic acid encoding a module from the 6-dEB gene cluster. However, the Office asserts that "knowledge regarding the nucleic acid encoding any gene cluster and the tolerance of all potential host cells to gene encoding molecular polyketide synthase" is not established.

While applicants are aware that previously issued patents do not have precedential force, it is interesting to point out the scope of the claims referred to in the issued patents where double-patenting is asserted. Claim 5 of the '491 patent reads on cells that would actually be produced by the claimed method without any limitation on the specific modular polyketide synthase module that

is to be inserted. The only limitation on the nature of the cell is that it has been modified to lack its own PKS gene cluster. Thus, the Office has, in the past, decided that the techniques described in the present application (the '491 patent issued based on a parent of the present case) would be equally applicable to modular PKS modules in general. As the Office agreed in the '491 case, the ability to modify a cell to express a heterologous expression system for a modular PKS module is new and applicable to modular PKS in general.

Similarly, claim 32 of the '731 patent (another patent issued on a parent of the present application) describes plasmids which contain an open reading frame of any PKS gene cluster.

As the Office points out, claim 1 of the '382 patent (also issued on a parent of the present application) is substantially identical to claim 1 presently presented except for the limitation of the modular PKS module to that of 6-dEB. There is no limitation whatsoever on the nature of the host cell. Again, in this case, the Office clearly recognized that the method of the invention was applicable to a wide range of host cells, not necessarily just those illustrated in the application.

Clearly, claim scope with respect to the nature of the modular PKS module and with respect to the nature of the host cell has not been a barrier to patentability based on parent applications herein. It is therefore unclear why, now, these issues arise.

With respect to the availability of nucleic acids encoding modular PKS modules, applicants respectfully point out that the invention does not lie in the nature of the nucleic acid or the module itself; rather, it lies in the ability to modify host cells with a heterologous expression system for a modular PKS. These methods and the resulting cells are workable for any modular PKS module; as more such modules become available, the methods of the invention may be applied to them without undue experimentation. Were applicants claiming the nucleic acid encoding a PKS module in

general, the point made by the Office would be more understandable. But the invention is directed elsewhere.

To use a somewhat hackneyed analogy, one might hypothesize an invention residing in the design of a jacket which fastens in a semi-circular pattern rather than in the usual manner. Would it be proper to limit the invention to the fasteners then available? That is not where the invention lies; it lies in the pattern of the fasteners, whatever they are. It would be unfair to limit the applicant only to those fasteners known at the time.

Similarly, here, the invention lies in modifying cells with a class of nucleic acids. The specific member of the class is irrelevant, just as the type of fastener is irrelevant in the example above.

With respect to the nature of the cells, applicants have stated generally on page 22 of the application that the host cells of the present invention can be derived from either prokaryotic or eukaryotic organisms; the cells that natively produce polyketides are merely preferred embodiments. In order to expedite prosecution, the claims have been limited to the types of cells that do generally product polyketides – *i.e.*, actinomycetes. Respectfully, the Office has not demonstrated any evidence that the methods claimed would be unworkable with cells other than *S. coelicolor*, especially as to actinomycetes in particular. Without such evidence, the scope asserted by applicants for the nature of the cells should prevail. It is not inherently incredible that transformed cells of actinomycetes, other than *S. coelicolor*, are obtainable by the claimed methods. No rationale has been stated for asserting that other cells cannot be useful in the invention. All that need result is that the inserted module be functional in catalyzing the synthesis of a polyketide. No reason or documentation is cited that this would not be the case for cells other than those illustrated.

Applicants also appreciate the recognition that patents issued to Katz, *et al.* – *i.e.*, U.S. Patent Nos. 5,824,513 and 6,004,787 – which rely on the disclosure of 17 January 1991, fail to teach heterologous expression of modular PKS. Rather, these patents describe manipulation of a modular PKS indigenous to the cell in which the manipulations take place. However, applicants note that claim 1 of the '787 patent reads on such manipulation independent of the source of the PKS-encoding nucleic acid.

For the reasons above, it is respectfully submitted that the rejection under 35 U.S.C. § 112, paragraph 1, may be withdrawn.

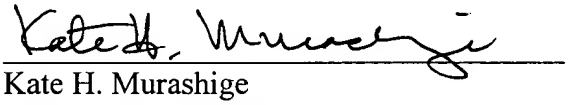
CONCLUSION

The rejections for double patenting have been addressed by submission of terminal disclaimers. The sole remaining rejection is under 35 U.S.C. § 112, paragraph 1 based on an assertion that the scope of the claims with regard to the PKS encoding nucleic acid and with respect to the cell into which it is introduced is too broad. The invention, however, is not directed to the nucleic acid itself, or to the cell itself, but rather a method to achieve their interrelationship. It is this method that constitutes the invention, not the individual participants in it. For this reason, applicants believe they should not be limited to any particular PKS encoding nucleic acid, as the invention is applicable to any such molecule, and should not be limited to a particular type of cell, as there is no evidence of record that the successful results achieved by applicants in *S. coelicolor* would not extrapolate to cells in general as asserted by applicants.

For this reason, applicants believe that claims 96-101 are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 300622000123.

Respectfully submitted,

Dated: January 13, 2005 By: 

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